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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/522,278	03/09/00	O HARE	P [illegible]

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EXAMINER	
ZARA, J	

ART UNIT	PAPER NUMBER
1635	11

DATE MAILED: 05/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/522,278	O HARE ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

This Office action is in response to the communication filed January 11, 2001, Paper No. 8.

Response to Amendment and Arguments

Withdrawn Objections and Rejections

Objection to claim 8 is withdrawn in light of Applicants' amendments filed January 11, 2001, Paper No. 8

Rejection of claims 18, 19, 22 and 23 under 35 U.S.C. 112, second paragraph, is withdrawn in light of Applicants' remarks and amendments filed January 11, 2001, Paper No. 8.

Rejection of claims 1-10 and 12-22 under 35 U.S.C. 103(a) as being unpatentable over O'Hare et al in view of Schwartz et al is withdrawn in light of Applicants' remarks filed January 11, 2001, Paper No. 8.

Rejection of claim 11 under 35 U.S.C. 103(a) as being unpatentable over O'Hare et al and Schwartz et al and further in view of Moyer et al is withdrawn in light of Applicants' remarks filed January 11, 2001, Paper No. 8.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the transport function of VP22" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 18 recites the limitation "the VP22" in line 5. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 9-12, 20 and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for aggregated compositions comprising the polypeptide of VP22 with known transport function and an oligonucleotide, and while being enabling for the delivery of peptides or polypeptides to target cells in vitro comprising linking these polypeptides to VP22 or to the fragments of VP22 known to have transport function, does not reasonably provide enablement for aggregated compositions comprising any and/or all polypeptides with the transport function of VP22 and further comprising polynucleotides (circular or linear) encoding full length proteins, or comprising polypeptides conjugated to any and/or all glycosides, nor enablement for a method of delivering polynucleotides or oligonucleotides to a cell in vitro or in vivo using these aggregated compositions, nor target cells which comprise such compositions,

which cells have been exposed to light whereby disaggregation was confirmed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to an aggregated composition comprising any and/or all polypeptides having the transport function of VP22, and which aggregated composition further comprises an oligonucleotide or polynucleotide, and which aggregated composition may further comprise polynucleotides (circular or linear) encoding full length proteins, or comprise fusion proteins, or comprise polypeptides conjugated to any glycosides, whereby the polynucleotides or oligonucleotides of the aggregated composition are targeted and appropriately delivered to a cell in vitro or in vivo, and which cells may be exposed to light to promote disaggregation of the aggregated composition.

The following factors have been considered in determining that the specification does not enable the skilled artisan to make and/or use the invention over the scope claimed.

The state of the prior art and the predictability or unpredictability of the art. The following references are cited herein to illustrate the state of the art of nucleic acid delivery in organisms. Branch and Crooke teach that the *in vivo* (whole organism) application of nucleic acids (such as antisense) is a highly unpredictable endeavor due to target accessibility and delivery issues. Crooke also points out that cell culture examples are generally not predictive of *in vivo* delivery and inhibition of target genes. (See entire text for Branch and especially pages 34-36 for Crooke).

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. Applicants have not provided guidance in the specification toward a method of forming aggregates comprising any and/or all targeting peptides which have the targeting function of VP22, and further comprising polynucleotides (circular or linear) encoding full length proteins, nor comprising fusion proteins, nor comprising polypeptides conjugated to any glycosides. Applicants have not provided guidance in the specification toward a method of delivering any polynucleotides or oligonucleotides to a target cell in vitro or in vivo comprising the administration of an aggregated composition comprising the targeting peptide sequences from VP22, nor of any and/or all homologues or members of the genus comprising polypeptides having the transport function of VP22, and which aggregated composition further comprises an oligonucleotide or polynucleotide, whereby the molecules of the aggregated composition are targeted and appropriately delivered to a cell in vitro or in vivo, and further whereby such cells are exposed to light to disaggregate the aggregates of the composition.

The specification teaches the preparation of aggregated compositions comprising various oligonucleotides which are linked to non-nucleic acid molecules via their 5' or 3' termini, and which oligonucleotides comprise between 20 and 50 nucleotides in length, and which optionally further comprise phosphorothioate internucleoside linkages, and which compositions further comprise any members of the genus comprising polypeptides with the targeting function of VP22, which polypeptides are optionally expressed in fusion with other amino acid sequences.

The specification fails to teach the successful delivery of oligonucleotides or any molecules to any target cells in vivo or in vitro comprising the administration of such aggregated compositions. The specification fails to teach the delivery of such compositions to a target cell and further whereby the cell has been exposed to light and disaggregation of the aggregated compositions has occurred. One skilled in the art would not accept on its face the examples given in the specification of the preparation of aggregated compositions comprising mixing oligonucleotides in combination with the targeting peptides from VP22, or VP22 fusion proteins as being correlative or representative of the ability to deliver oligonucleotides or polynucleotides to a target cell in vivo or in vitro comprising the administration of aggregated compositions comprising the transport sequences of VP22, or any homologues or members of the genus comprising polypeptides with the transport function of VP22, and which compositions further comprise polynucleotides in vitro or in vivo in view of the lack of guidance in the specification and known unpredictability associated with the administration and successful delivery of nucleic acids to a target cell in vitro or in vivo using the aggregated compositions described above, including compositions comprising any homologue or member of the genus comprising polypeptides with the transport function of VP22. The specification as filed fails to provide any particular guidance or adequate description of the elements which are essential, or indicate what distinguishing attributes are concisely shared by the members of the genus comprising polypeptides with the transport function of VP22. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of

structural differences between members of the genus is permitted. Furthermore, the specification as filed fails to provide any particular guidance which resolves the known unpredictability in the art associated with in vitro or in vivo delivery of any and/or all molecules including antisense or ribozymes using the aggregated compositions disclosed.

The breadth of the claims and the quantity of experimentation required. The claims are drawn to aggregated compositions comprising any and/or all polypeptides with the transport function of VP22 and further comprising polynucleotides (circular or linear) encoding full length proteins, or comprising fusion proteins, or comprising polypeptides conjugated to any glycosides. The claims are further drawn to an aggregated composition comprising the transport polypeptide of VP22 and further comprising an oligonucleotide or polynucleotide, whereby the polynucleotides or oligonucleotides of the aggregated composition are targeted and appropriately delivered to a cell in vitro or in vivo. In order to practice the invention over the scope claimed, it would require undue trial and error and undue experimentation beyond which is taught in the specification to practice the invention drawn to methods of delivering an oligonucleotide or polynucleotide to a target cell in vivo or in vitro comprising the administration of aggregated compositions comprising any and/or all polypeptides with the transport function of VP22 and further comprising an oligonucleotide or polynucleotide. The quantity of experimentation required to practice the invention as claimed would require the disclosure of the common attributes or characteristics concisely identifying members of the genus comprising polypeptides with the transport function of VP22. One of skill in the art would reasonably conclude that the

disclosure fails to provide a representative number of species to describe this genus claimed. Furthermore, the quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of methods for forming aggregates comprising any polypeptide with the transport function of VP22 and further comprising polynucleotides (circular or linear) encoding full length proteins, or comprising fusion proteins, or comprising polypeptides conjugated to any glycosides. The quantity of experimentation required to practice the invention as claimed would also require the *de novo* determination of methods for obtaining target cell delivery in vitro and in vivo using the compositions claimed. Since the specification fails to provide any particular guidance for the successful delivery of oligonucleotides or polynucleotides to any target cells in vitro or in vivo using the aggregated compositions claimed, and since determination of the factors necessary for target cell delivery in vivo or in vitro is highly unpredictable, it would require undue experimentation to practice the invention over the scope claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 1, 2, 5-8, 13-16, 18-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Langel et al.

Langel et al teach the delivery of aggregated compositions to target cells in vitro and in vivo, which compositions comprise a polypeptide having a transport function of VP22, which transport function comprises intracellular transport, and which compositions further comprise an antisense oligonucleotide in a ratio of at least 1:1 with the transport polypeptide, which antisense oligonucleotide comprises at least 10 nucleotides and further comprises phosphorothioate internucleoside linkages and optionally may comprise a detectable label or a cleavable linkage, and which aggregated particles are between 0.1 and 5 microns (See especially abstract; columns 5, 6, 9, 13, 15, 16, examples 4, 6 and 8 in columns 19-22).

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

ANDREW WANG
PATENT EXAMINER
TC 1600

JZ

May 9, 2001